New diseases

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New diseases; old evolutionary battles

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New or re-emerging infectious diseases appear to be on the increase and are major threats to humanity both directly, through infection, and indirectly through reducing agricultural production. For example, the novel human pathogens HIV, SARS, and the H5N1 strain of Influenza A have evolved in recent years; major killers such as tuberculosis and malaria are rising dramatically even after apparent successful campaigns in the last century; and other diseases have arisen in new places, such as the outbreak of West Nile Virus in North America. In the UK, we are all too aware of the threat posed to livestock by the Bluetongue Virus and the spread of Bovine TB. Patterns of crop diseases are also changing; for example, wheat rusts from Africa are now threatening European agriculture.

Of course, changes in pathogens, parasites and consequent patterns of disease are not new; parasites are in a constant evolutionary battle with their hosts that can lead to complex dynamics over time. But what has changed due to human activities, and very rapidly in evolutionary time, is the physical environment, density and 'connectedness' of hosts. Connectedness and density will not be discussed; here I deal with environmental change. Due to intense natural selection, pathogens and parasites respond quickly to environment changes and we should therefore not be surprised that new threats are emerging. In addition to the science needed to new treatments, we urgently need also to find ways of mapping these threats in relation to the environment and predicting their future distribution. More generally, the problem of scaling from small-scale biological processes to the larger aspects of landscapes and regional climate change is one common to many challenges facing policy makers. This is where the landscape ecology work in IBERS comes in.

Take, for example, our studies of vector-borne diseases (VBD). These are diseases, such as bluetongue, where the parasite has life stages in two different hosts and where one, the 'vector', often an insect, transmits infectious stages to the other, say a bird or mammal. Temperature and rainfall have a strong influence on insect rate of development and populations; a recent mathematical study indicated that even very small increases in temperature can be amplified by vector population dynamics to strongly affect transmission. This is why VBD are particularly prone to changes in climate and why climate change is a cause of such concern.

Parasites are under strong evolutionary pressure to adapt to the host's defences and transmission systems have often become very tightly coupled between specific vectors and hosts. A good example is malaria, a vector-borne disease caused by protozoan parasites. These microscopic animals have life-stages in blood-feeding insects such as mosquitoes and midges and in the vertebrates that these flies bite, including lizards, birds and mammals. Different species of malaria parasite are usually very specifically associated with certain vectors and hosts. There are hundreds, if not tens of thousands, of different species of avian malaria parasites; one study has suggested that almost every species of bird, of which there are over 10,000, will have at least one malaria species and the same could be true for other groups. Prevalence levels can be very high: in a study in an Oxfordshire wood, a quarter of the blue tits were infected. Human malaria transmission is highly specific. Four species of malaria parasite are specific to humans, of which two cause serious disease. The vectors in this case are exclusively Anopheline mosquitoes with about 70 of the 380 recorded species worldwide competent for transmission. Transmission levels can vary over very short distances in many vector-borne systems; the key here is to understand how local environment can influence the density of vectors and how they disperse when seeking blood meals.

In IBERS, we are working on how the environment influences transmission of human malaria in Africa and how climate change may alter the dynamics by using a combination of field measurements and mathematical modelling. Human malaria still causes devastating mortality and sickness, particularly in Africa where between 1-2 million children are estimated to die of the disease annually (**Figure 1**).

Figure 1. *Mother with baby in Tanzania. (Photo by Chris Thomas)*

In IBERS, we are taking a spatial, landscape ecology approach to understand how landscape structure affects transmission, particularly for features we can manage such as land-use and irrigation. This is a fine scale landscape process; work in The Gambia showed there can be a 20-fold difference in average number of infectious bites per person over only 10 kilometers, due to variation in the distribution of mosquito breeding areas. In Africa, the main vector is a small mosquito called *Anopheles gambiae* (**Figure 2**). This species is highly adapted to feed on humans and is one of the world's most efficient vectors. As ecologists, our challenge is to measure features in the landscape specific to this very particular insect, including the distribution and activities of humans, and relate this to infection levels and clinical disease. *Anopheles gambiae* presents us with quite a challenge as she lays her eggs in temporary, rain-fed puddles, pools, irrigation and overspills. These are often small features in a landscape and Africa is a very big place! This is where satellite mapping and spatial ecology comes into play.

Figure 2. Anopheles gambiae *mosquito.*

One key gap in our knowledge is how variation in rainfall affects transmission. In Africa, rainfall is often patchy and varies a great deal between seasons and years. Ideally we would need a series of satellite images to measure these changes over time. However, sensors on Landsat and SPOT are passive 'optical', measuring reflected light from the ground in wavelengths from UV, visible and thermal bands. These wavelengths reflect off the top of clouds (if you have flown in an aircraft into the bright light above the clouds you will appreciate this). In other words, these sensors can't 'see' (more formally, acquire data) through the clouds – a real problem in an African rainy season. For this reason we have recently turned to radar remote sensing.

The European Space Agency's Envisat satellite (**Figure 3**) is equipped with active radar instruments that send a focused burst of microwave light to the earth below. The sensors then measure the absorption and scattering of this energy. The data images produced are much more difficult to interpret than optical imagery, but they can tell us a great deal that would be unavailable by any other means. Radar remote sensing is a new frontier in ecology and it promises a great deal. For example, using optical imagery we can map woodland, but with radar we can also measure tree structure and estimate biomass. Envisat's radar sensor is highly sensitive to water and the longer wavelengths penetrate clouds, making this a potentially powerful new tool for malaria mapping.

Figure 3. *Envisat satellite. (ESA public library).*

We have investigated this potential as part of a study in Tanzania funded by ESA and the US National Institutes of Health. Here we have been able to build up a monthly time-series of maps measuring the presence of water for mosquito breeding for every 30 m square in an area of 150 km x 150 km. For the first time, we have captured the dynamics of the landscape important to malaria mosquitoes and can now couple this with more sophisticated mathematical models of mosquito populations and their movements. It is early in the project, but results look promising. One notable finding has been the discovery of so-called 'dry-season refugia'; small perennial wetland areas where mosquito populations can 'tick-over' during the dry season . It is hypothesized that mosquito populations grow from these areas when the rains come and create breeding sites across the landscape (**Figure 4**).

We speculate that it may be more effective to apply larvicide to these refugia in the dry season, to kill mosquitoes and impede their population growth at this population bottleneck, rather than wait until the malaria season that follows the rains. We often talk about waging war on malaria. Using this analogy, IBERS spatial ecology can tell us where the enemy is to help us plan how best to go on the attack (**Figure 5**).

Figure 4. *Chris Thomas sampling mosquito larvae in a Tanzanian rice field. (Photo by Rachel Bott).*

Like many VBD, the distribution of malaria in Africa is likely to be shifting in response to climate change. Indeed, this process is possibly already underway but there are many other changes taking place in the region and it is difficult to tease apart independent effects. Nevertheless, we have used continental-scale climate models of malaria across Africa to estimate these range shifts. We project that epidemics may become more likely in highland regions such as Ethiopia, the Kenyan and Tanzanian highlands, Rwanda and Burundi, putting tens of millions more people at risk of the disease. Our work suggests that, in addition to combatting malaria where it currently occurs, effort should also be directed into these new vulnerable areas to counter these potential changes: for once, we may be able to get ahead of the epidemic curve. Climate models are very coarse grain and it is unlikely that they will have a resolution finer than 10-20 km in the foreseeable future. While this is an appropriate resolution for distribution of resources on a regional or national level, it cannot help the planning needed at the local level for effective interventions, such as bed nets, health education, environmental management, DDT, health services, drug delivery and, potentially, vaccines. Here we hope our landscape hazard mapping

Figure 5. On fieldwork in the Kilombero Valley, Tanzania. (Photo by Christine Dunn)

will be important, as we can link features of the landscape to potential changes arising from increased temperature and changed patterns of rainfall.

At a fundamental level, this work will help us to understand the complexity of transmission and the evolutionary forces involved; knowledge that may help us plan new interventions. And it is not just for malaria. We believe our general approach is likely to be applicable to other vector-borne diseases such as bluetongue and other pathogens that have an environmental phase, such as bovine TB.

In the year of Darwin's 200th anniversary, it is worth noting that many of the urgent problems and opportunities arising from environmental change need to be considered at the landscape level, including new and emerging diseases. Spatial ecology and evolution, although a relatively new combined discipline made possible by advances in technology, is showing just how important the landscape context can be. In the famous last paragraph to the Origin of Species, Darwin invites us to contemplate the complexity of life in a tangled bank. A good start is to look at the land on either side.

\\ A grain in the balance will determine which individual shall live and which shall die, - which variety or species shall increase in number, and which shall decrease, or finally become extinct. As the individuals of the same species come in all respects into the closest competition with each other, the struggle will generally be most severe between them; it will be almost equally severe between the varieties of the same species, and next in severity between the species of the same genus. But the struggle will often be very severe between beings most remote in the scale of nature. The slightest advantage in one being, at any age or during any season, over those with which it comes into competition, or better adaptation in however slight a degree to the surrounding physical conditions, will turn the balance. //

Darwin - The Origin of Species